Refine Search

Search Results -

Term	Documents
E2	72292
E2S	251
(3 SAME E2).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	24
(L3 SAME (E2)).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	24

Database: US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L4

Refine Search | Recall Text | Clear | Interrupt

Search History

DATE: Friday, January 16, 2004 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES; OP=AND			
L4	L3 same (E2)	24	L4
L3	L2 same (treat or inhibit)	268	L3
L2	((hepatitis adj C) or HCV) same (bind or binding or receptor)	1449	L2
DB=PGPB,USPT,EPAB,JPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES; OP=AND			
L1	Worman-Howard-J$.in.	3	L1

END OF SEARCH HISTORY

PALM INTRANET

Day : Friday
Date: 1/16/2004

Time: 09:18:41

Inventor Name Search

Enter the **first few letters** of the Inventor's Last Name.
Additionally, enter the **first few letters** of the Inventor's First name.

Last Name	**First Name**	
Worman	Howard	Search

To go back use Back button on your browser toolbar.

Back to PALM | ASSIGNMENT | OASIS | Home page

```
alpha interferon--pharmacology--pd; ribavirin--drug combination--cb;
ribavirin--drug *therapy*--dt; ribavirin--pharmacology--pd
MEDICAL DESCRIPTORS:
carcinogenesis; hepatitis non A non B--drug *therapy*--dt; hepatitis non A
non B--etiology--et; virus excretion; liver cirrhosis--complication--co;
liver cell carcinoma--complication--co; lymphoproliferative disease
--etiology--et; disease association...

...lymphocyte; lymphocyte proliferation; phenotype; immunoglobulin variable
region; antibody production; drug response; precancer; cell clone;
malignant transformation; lymphocyte activation; cell surface; protein
binding; spleen cancer--drug *therapy*--dt; antigen expression; antigen
binding; human; review; priority journal
?ds

Set     Items   Description
S1       3365   ((HEPATITIS (W) C) OR HCV) (S) (BIND OR BINDING OR INHIBIT
            OR INHIBITOR)
S2          0   S1 (S) (E2)
S3        149   S1 (S) (ENVELOPE (W) PROTEIN?)
S4         13   S3 AND (TREAT OR THERAPY)
S5          8   RD (unique items)
?s s3 and (yeast (w) hybrid)
             149  S3
          257743  YEAST
          173428  HYBRID
             157  YEAST(W)HYBRID
      S6       0  S3 AND (YEAST (W) HYBRID)
?s s3 and (E2 (w) binding)
>>>"E2" does not exist
             149  S3
               0  E2
         1800155  BINDING
               0  E2(W)BINDING
      S7       0  S3 AND (E2 (W) BINDING)
?ds

Set     Items   Description
S1       3365   ((HEPATITIS (W) C) OR HCV) (S) (BIND OR BINDING OR INHIBIT
            OR INHIBITOR)
S2          0   S1 (S) (E2)
S3        149   S1 (S) (ENVELOPE (W) PROTEIN?)
S4         13   S3 AND (TREAT OR THERAPY)
S5          8   RD (unique items)
S6          0   S3 AND (YEAST (W) HYBRID)
S7          0   S3 AND (E2 (W) BINDING)
?logoff
       16jan04 09:30:17 User259876 Session D583.2
            $2.75    0.859 DialUnits File155
               $1.47  7 Type(s) in Format  3
            $1.47  7 Types
     $4.22  Estimated cost File155
            $4.63    0.827 DialUnits File5
     $4.63  Estimated cost File5
            $7.42    0.757 DialUnits File73
               $2.70  1 Type(s) in Format  3
            $2.70  1 Types
    $10.12  Estimated cost File73
            OneSearch, 3 files,  2.443 DialUnits FileOS
     $1.62  TELNET
    $20.59  Estimated cost this search
    $21.06  Estimated total session cost   2.535 DialUnits


### Status: Signed Off. (8 minutes)
```

Status: Path 1 of [Dialog Information Services via Modem]

Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ******** HHHHHHHH SSSSSSSS?
Status: Signing onto Dialog
 ****
ENTER PASSWORD:
 ******** HHHHHHHH SSSSSSSS? ********
Welcome to DIALOG
Status: Connected

Dialog level 03.06.02D

Last logoff: 15jan04 08:23:01
Logon file001 16jan04 09:22:47
*** ANNOUNCEMENT ***
***
--File 654 - US published applications from March 15, 2001 to the present are now online. Please see HELP NEWS 654 for details.

***
--File 581 - The 2003 annual reload of Population Demographics is complete. Please see Help News581 for details.

***
--File 990 - NewsRoom now contains February 2003 to current records.
File 992 - NewsRoom 2003 archive has been newly created and contains records from January 2003. The oldest months's records roll out of File 990 and into File 992 on the first weekend of each month.
To search all 2003 records BEGIN 990, 992, or B NEWS2003, a new OneSearch category.
***
--Connect Time joins DialUnits as pricing options on Dialog.
See HELP CONNECT for information.
***
***
--SourceOne patents are now delivered to your email inbox as PDF replacing TIFF delivery. See HELP SOURCE1 for more information.
***
--Important news for public and academic libraries. See HELP LIBRARY for more information.
***
--Important Notice to Freelance Authors--
See HELP FREELANCE for more information
***
NEW FILES RELEASED
***DIOGENES: Adverse Drug Events Database (File 181)
***Emergency Room (File 454), Hospital Inpatient Profiles (File 462), and Hospital Outpatient Profiles (File 463)
***World News Connection (File 985)
***Dialog NewsRoom - 2003 Archive (File 992)
***TRADEMARKSCAN-Czech Republic (File 680)
***TRADEMARKSCAN-Hungary (File 681)
***TRADEMARKSCAN-Poland (File 682)
***
UPDATING RESUMED
***
RELOADED
***Population Demographics -(File 581)

```
***CLAIMS Citation (Files 220-222)

REMOVED
                    ***

      >>> Enter BEGIN HOMEBASE for Dialog Announcements <<<
      >>>    of new databases, price changes, etc.      <<<
                    ****
KWIC is set to 50.
HILIGHT set on as '*'
* * * ALL NEW CURRENT YEAR RANGES HAVE BEEN * * *
* * * INSTALLED   * * *

File   1:ERIC  1966-2004/Jan 06
       (c) format only 2004 The Dialog Corporation

      Set  Items  Description
      ---  -----  -----------
Cost is in DialUnits
?b 155, 5, 73
       16jan04 09:23:30 User259876 Session D583.1
            $0.32    0.092 DialUnits File1
     $0.32  Estimated cost File1
     $0.15  TELNET
     $0.47  Estimated cost this search
     $0.47  Estimated total session cost   0.092 DialUnits


SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-2004/Jan W2
        (c) format only 2004 The Dialog Corp.
*File 155: Medline is updating again (12-22-2003).
Please see HELP NEWS 154, for details.
  File   5:Biosis Previews(R)  1969-2004/Jan W2
        (c) 2004 BIOSIS
  File  73:EMBASE  1974-2004/Jan W2
        (c) 2004 Elsevier Science B.V.
*File  73: New prices as of 1-1-04 per information provider
request. See ?RATES 73

      Set  Items  Description
      ---  -----  -----------
?s ((hepatitis (w) C) or HCV) (s) (bind or binding or inhibit or inhibitor)
         305235  HEPATITIS
        2945627  C
          83313  HEPATITIS(W)C
          44878  HCV
         245181  BIND
        1800155  BINDING
         379640  INHIBIT
         894775  INHIBITOR
      S1    3365  ((HEPATITIS (W) C) OR HCV) (S) (BIND OR BINDING OR
                  INHIBIT OR INHIBITOR)
?s s1 (s) (E2)
>>>"E2" does not exist
           3365  S1
              0  E2
      S2      0  S1 (S) (E2)
?s s1 (s) (envelope (w) protein?)
Processing
           3365  S1
          87017  ENVELOPE
        4469497  PROTEIN?
      S3    149  S1 (S) (ENVELOPE (W) PROTEIN?)
?s s3 and (treat or therapy)
            149  S3
         142937  TREAT
```

```
        4886017  THERAPY
     S4      13  S3 AND (TREAT OR THERAPY)
?rd
...completed examining records
     S5       8  RD (unique items)
?t s5/3,k/all
```

5/3,K/1 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

11855644 99296734 PMID: 10366577

Broadly cross-reactive, high-affinity antibody to hypervariable region 1 of the hepatitis C virus in rabbits.

Shang D; Zhai W; Allain J P
Department of Haematology, University of Cambridge, Cambridge, United Kingdom.

Virology (UNITED STATES) Jun 5 1999, 258 (2) p396-405, ISSN 0042-6822 Journal Code: 0110674
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The HCV hypervariable region 1 (HVR1) of the main E2 *envelope* *protein* is critically important in *HCV* neutralization but its extreme variability makes immune *therapy* and vaccine development particularly difficult. To explore the hypothesis that HVR1 carries a common epitope susceptible of eliciting cross-reactive neutralizing and inhibitory antibodies, rabbits...

... 16 of 17 unrelated HVR1 peptides; (3) antibodies appeared of restricted diversity irrespective of the linear HVR1 peptide sequences; (4) anti-HVR1 peptides effectively captured *HCV* in 22 of 33 plasmas from random infected patients; (5) anti-HVR1 IgG blocked the *binding* of antibody-captured *HCV* to MOLT-4 cells. These findings suggest that with an appropriate HVR1 peptide immunization scheme, high titer, broadly cross-reactive, blocking antibodies to *HCV* can be produced. Antibodies to the putative ubiquitous HVR1 epitope may have important clinical uses.

5/3,K/2 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

11432439 98315045 PMID: 9649423

Towards a solution for hepatitis C virus hypervariability: mimotopes of the hypervariable region 1 can induce antibodies cross-reacting with a large number of viral variants.

Puntoriero G; Meola A; Lahm A; Zucchelli S; Ercole B B; Tafi R; Pezzanera M; Mondelli M U; Cortese R; Tramontano A; Galfre' G; Nicosia A
Istituto di Ricerche di Biologia Molecolare P.Angeletti, Via Pontina Km 30.600, 00040 Pomezia (Roma).

EMBO journal (ENGLAND) Jul 1 1998, 17 (13) p3521-33, ISSN 0261-4189 Journal Code: 8208664
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The hypervariable region 1 (HVR1) of the putative *envelope* *protein* E2 of *hepatitis* *C* virus (*HCV*) is the most variable antigenic fragment in the whole viral genome and is mainly responsible for the large inter-and intra-individual heterogeneity of the...

... escape from host immune response. Since anti-HVR1 antibodies are the

only species shown to possess protective activity up to date, developing an effective prevention *therapy* is a very difficult task. We have approached the problem of HVR1 variability by deriving a consensus profile from >200 HVR1 sequences from different viral...

... M13 bacteriophage. This library was affinity selected using many different sera from infected patients. Phages were identified which react very frequently with patients' sera and *bind* serum antibodies that cross-react with a large panel of HVR1 peptides derived from natural *HCV* variants. When injected into experimental animals, the 'mimotopes' with the highest cross-reactivity induced antibodies which recognized the same panel of natural HVR1 variants. In...

... we identified a sequence pattern responsible for the observed cross-reactivity. These data may hold the key for future development of a prophylactic vaccine against *HCV*.

5/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11342813 98222877 PMID: 9563413
Transmission of hepatitis G virus in patients with angioedema treated with steam-heated plasma concentrates of C1 inhibitor.
De Filippi F; Castelli R; Cicardi M; Soffredini R; Rumi M G; Silini E; Mannucci P M; Colombo M
Angela Maria e Antonio Migliavacca Center for Liver Disease, Department of Internal Medicine, Istituto di Ricovero e Cura a Carattere Scientifico Maggiore Hospital, University of Milan, Italy.
Transfusion (UNITED STATES) Mar 1998, 38 (3) p307-11, ISSN 0041-1132 Journal Code: 0417360
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

...INH deficiency (19 who received unmodified C1-INH concentrates, 23 who received steam-heated concentrates, and 42 untreated patients) were tested for HGV RNA and *hepatitis* *C* virus (*HCV*) RNA by a nested polymerase chain reaction (PCR). The samples were also tested for antibodies to the E2 *envelope* *protein* of HGV (anti-HGV) and to *HCV* with enzyme-linked immunosorbent assays. RESULTS: Nine (11%) patients had serum HGV RNA; that is, 7 (17%) of 42 patients previously treated with C1-INH...

... 60). Anti-HGV was more common among the recipients of unmodified concentrates than among those given steam-heated concentrates (26 vs. 0%, p = 0.014). *HCV* RNA was more frequently detected in treated patients than in untreated patients (33 vs. 7%, p = 0.005) and in the 19 recipients of unmodified...

... with steam-heated concentrates (58 vs. 16%, p = 0.003). Only one HGV RNA-seropositive patient had elevated serum aminotransferase activity, compared to 11 with *HCV* RNA. CONCLUSION: HGV was transmitted by both unmodified and steam-heated concentrates, but it caused persistent viremia in a minority of the cases and was...
Descriptors: Angioneurotic Edema--drug *therapy*--DT; *Complement 1 Inactivators--administration and dosage--AD; *Flaviviridae; *Hepatitis, Viral, Human--transmission--TM

5/3,K/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10107232 22070218 PMID: 12075086
Detection of neutralizing antibodies to hepatitis C virus using a biliary

cell infection model.
Bichr Saadia; Rende-Fournier Rosanna; Vona Giovanna; Yamamoto Ana-Maria; Depla Erik; Maertens Geert; Brechot Christian
Inserm U370, Faculte de Medecine Necker, 156 rue de Vaugirard, 75730 Paris Cedex 15, France.
Journal of general virology (England) Jul 2002, 83 (Pt 7) p1673-8, ISSN 0022-1317 Journal Code: 0077340
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The identification and characterization of neutralizing anti-*hepatitis* *C* virus (*HCV*) antibodies may have a major impact on understanding *HCV* pathogenesis. However, to date, their detection has only been based on the inhibition of either the E2 *envelope* *protein* or *HCV* virions *binding* to different target cells. The permissiveness of primary biliary cells for *HCV* infection has been demonstrated previously. In the present report, infection of biliary cells was demonstrated further by combining PCR and immunohistochemical detection of the *HCV* core protein. This study demonstrates, using both serum and purified IgG, the presence of neutralizing anti-*HCV* antibodies in the serum of patients showing long-term response to antiviral *therapy*. Overall, the usefulness of the primary biliary cell infection model to investigate anti-*HCV* neutralization is shown.

5/3,K/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10030072 21965448 PMID: 11968795
[Recent advances of basic research and clinical application of lactoferrin as an antiviral reagent against chronic hepatitis C]
Nozaki Akito; Tanaka Katsuaki; Naganuma Atsushi; Kato Nobuyuki
Department of Molecular Biology, Okayama University Graduate School of Medicine and Dentistry.
Nippon rinsho. Japanese journal of clinical medicine (Japan) Apr 2002, 60 (4) p819-29, ISSN 0047-1852 Journal Code: 0420546
Document type: Journal Article; Review; Review, Tutorial ; English Abstract
Languages: JAPANESE
Main Citation Owner: NLM
Record type: Completed

... virus(HCV), discovered in 1989, is the major causative agent of chronic viral hepatitis. Most patients progress to liver cirrhosis and hepatocellular carcinoma. In the *therapy* of hepatitis C, only interferon has been used effectively as an anti-HCV reagent in Japan, but its effectiveness is limited to about 30% of...

... Further analysis found that the carboxyl region of lactoferrin, which partially shows amino acid sequence homology to human CD81, specifically bound to the HCV E2 *envelope* *protein*, and identified a 33 amino acids as a critical *binding* domain of lactoferrin. On the other hand, it has been shown that bovine lactoferrin was effective in some patients with chronic hepatitis received an 8-week course of lactoferrin treatment. Further clinical trials showed that lactoferrin is a promising candidate for adjuvant *therapy* with interferon in patients with chronic *hepatitis* *C*.
Descriptors: Hepatitis C, Chronic--drug *therapy*--DT; *Lactoferrin --therapeutic use--TU; Antigens, CD--chemistry--CH; Clinical Trials; Drug *Therapy*, Combination; Interferon-alpha--therapeutic use--TU; Lactoferrin --chemistry--CH; Lactoferrin--metabolism--ME; Protein Binding; Sequence Homology, Amino Acid; Viral Envelope Proteins--metabolism--ME

5/3,K/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09763812 21568394 PMID: 11711631

Production and characterization of monoclonal antibodies specific for a conserved epitope within hepatitis C virus hypervariable region 1.

Li C; Candotti D; Allain J P
National Blood Service, Division of Transfusion Medicine, East Anglia Blood Centre, Cambridge CB2 2PT, United Kingdom.

Journal of virology (United States) Dec 2001, 75 (24) p12412-20, ISSN 0022-538X Journal Code: 0113724
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Frequent mutations in hypervariable region 1 (HVR1) of the main *envelope* *protein* of *hepatitis* *C* virus (*HCV*) is a major mechanism of persistence by escaping the host immune recognition. HVR1 contains an epitope eliciting neutralizing antibodies. This study was aimed to prepare broadly cross-reacting, high-affinity, monoclonal antibodies (MAb) to the HVR1 C terminus of *HCV* with potential therapeutic neutralizing capacity. A conserved amino residue group of glycine (G) at position 23 and glutamic acid (Q) at position 26 in HVR1...
... G1 kappa chain [IgG1(kappa)], cross-reacted with 32 and 30 of 39 random C-terminal HVR1 peptides, respectively, and did not react with other *HCV* peptides. The V(H) of 2P24 and 15H4 heavy chains originated from Igh germ line v gene family 1 and 8, respectively. In contrast, the...

...10(-8) M with two nonimmunizing HVR1 peptides) paralleled the reactivity obtained with peptide enzyme immunoassay. MAbs 2P24 and 15H4 captured 25 of 31 (81%) *HCV* in unselected patients' plasmas. These antibodies also blocked *HCV* *binding* to Molt-4 cells in a dose-dependent fashion. The data presented suggest that broadly cross-reactive MAbs to a conserved epitope within *HCV* HVR1 can be produced. Clinical application for passive immunization in *HCV* -related chronic liver disease and after liver transplantation is considered.
; Amino Acid Sequence; Antibodies, Monoclonal--biosynthesis--BI; Antibodies, Monoclonal--chemistry--CH; Antibody Affinity; Epitopes; Hepatitis C--*therapy*--TH; Molecular Sequence Data; Vaccination; Viral Hepatitis Vaccines--therapeutic use--TU; Viral Proteins--analysis--AN

5/3,K/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08833297 20117181 PMID: 10653456

Hepatitis C--virology and future antiviral targets.

Di Bisceglie A M
Department of Internal Medicine, Saint Louis University School of Medicine, Missouri 63104, USA.

American journal of medicine (UNITED STATES) Dec 27 1999, 107 (6B) p45S-48S, ISSN 0002-9343 Journal Code: 0267200
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The *hepatitis* *C* virus is a single-stranded RNA virus with a genome approximately 9,000 nucleotides in length. The genome consists of a single, large open reading...

...stable secondary structure. The ORF codes form a single polyprotein that is processed into as many as 10 polypeptides, including a capsid protein (core), two *envelope* *proteins* (E1 and E2), and nonstructural proteins

(NS2, NS3, NS4, and NS5). Potentially suitable antiviral targets include the IRES, protease, helicase, and RNA polymerase. In vitro studies show that antisense oligonucleotides can *inhibit* the production of structural *HCV* proteins and may be therapeutically useful if the problems of stability and delivery can be solved. The *binding* of *HCV* *envelope* *proteins* to CD81, a potential receptor for viral entry into hepatocytes, has recently been described and also raises the possibility of agents to block the *binding* to CD81 or the entry of the virus into cells.
; Drug Design; Hepacivirus--drug effects--DE; Hepacivirus--physiology --PH; Hepatitis C--drug *therapy*--DT; Hepatitis C--virology--VI; Virus Replication

5/3,K/8 (Item 1 from file: 73)

12099527 EMBASE No: 2003210462
Hepatitis C virus (HCV) and lymphomagenesis
Weng W.-K.; Levy S.
S. Levy, Department of Medicine, Division of Oncology, Stanford University Sch. of Medicine, Stanford, CA 94305 United States
Leukemia and Lymphoma (LEUK. LYMPHOMA) (United Kingdom) 01 JUL 2003, 44/7 (1113-1120)
CODEN: LELYE ISSN: 1042-8194
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 77

Hepatitis C virus (*HCV*) is the major cause for non-A, non-B hepatitis. Most *HCV*-infected individuals do not clear the virus resulting in a chronic infection that may potentially lead to liver cirrhosis and hepatocellular carcinoma. In addition to hepatic manifestations, *HCV* infection is associated with B cell lymphoproliferative disorders, including mixed cryoglobulinemia, usually a benign condition, and overt B cell lymphoma. A direct role of *HCV* infection in the genesis of these B cell lymphoproliferative disorders has been suggested initially by epidemiological studies and is supported by recent studies, which analyzed the monoclonal B cells that proliferate in these disorders. How *HCV* induces B cell lymphoproliferative disorders is still unclear, it is probably not due to direct change of phenotype in B cells after viral infection, but may be due to an *HCV*-antigen driven process. Support for this hypothesis comes from the analysis of monoclonal B cells found in these disorders, which use a restricted repertoire of immunoglobulin variable region genes that are similar to those used by B cells that secrete anti-*HCV* antibodies. The fact that monoclonal IgM is resolved in *HCV*-infected patients who responded to anti-viral treatment supports the linkage between antigen persistence and B cell proliferation. Finally, the linkage between benign B cell...

...that subsequently converted to an overt B cell lymphoma. The molecular basis for viral induced B cell proliferation is still unknown. One possibility is that *HCV* stimulates the proliferation of monoclonal B cells via their *HCV*-specific B cell receptor (BCR) on the cell surface. *Binding* of the *HCV* *envelope* *proteins* to a cellular ligand, CD81, may also enhance this antigen-driven process. A recent report on regression of splenic marginal zone lymphoma after anti-viral treatment with interferon and ribavirin has significantly strengthened the cause-effect relationship between *HCV* infection and lymphoma. Further studies should determine whether BCRs expressed on *HCV*-associated lymphomas, particularly those that regress in response to anti-viral *therapy*, *bind* *HCV* antigens that stimulate their proliferation.
DRUG DESCRIPTORS:
hepatitis C antibody--endogenous compound--ec; antivirus agent--drug *therapy*--dt; antivirus agent--pharmacology--pd; B lymphocyte receptor --endogenous compound--ec; CD81 antigen--endogenous compound--ec; alpha interferon--drug combination--cb; alpha interferon--drug *therapy*--dt;